

Suppl. Figures Legends

S1 Fig. Platelet or platelet supernatant increases DV2 replication in THP-1 cells *in vitro*. **A.** Quantification of viral dsRNA in DV-infected THP-1 cells. A similar study was performed as mentioned in Fig. 1 using THP-1 cells. THP-1 cells were stained for intracellular dsRNA (pink, Cy5) and nucleus (blue, DAPI), bars 5 μm . **B.** The mean fluorescence intensity (MFI) for dsRNA was quantified from 25 such images (mentioned in Suppl. Fig. 1A) from each above experiment in triplicate and mentioned as mean \pm SEM. One-Way ANOVA with multiple comparison test was used,, *** $p < 0.0001$.

S2 Fig. Gating strategy for detecting intracellular NS1 (viral) and CD41 (platelet) in monocytes. As mentioned in Fig. 1D-E, after the treatment the monocytes were labeled for detecting intracellular NS1 and CD41.

S3 Fig. RhPF4 increases DV2 replication in THP-1 cells. **A.** As mentioned in Fig. 2B-C, a similar experiment was performed using THP-1 cells. **B.** Data were calculated as mentioned in Fig. 2B-C; *** $p < 0.0001$, ns = non-significant compared to THP-1 treated with DV2.

S4 Fig. Anti-PF4 antibody abrogates platelet-mediated DV2 replication in THP-1 cells. As mentioned in the Fig. 2H-I, a similar experiment was performed using THP-1 cells. The dsRNA was measured using microscopy, bars in images $\sim 5 \mu\text{m}$. **B.** MFI of dsRNA was measured from Suppl. Fig. 7A and analyzed, *** $p < 0.01$.

S5 Fig. AMG487 decreases PF4-mediated DV2 replication THP-1 cells. **A.** As mentioned in Fig. 2F-G, a similar experiment was performed to determine the effective concentration of AMG487. The DV2-infected THP-1 cells were incubated with two different concentrations of AMG487 (1 and 2.5 μM) for 10 min before adding PF4. The dsRNA was measured using microscopy, bars in images $\sim 5 \mu\text{m}$. **B.** MFI of dsRNA was measured from Suppl. Fig. 4A and analyzed, *** $p < 0.0001$, ** $p = 0.0061$, ns= non-significant.

S6 Fig. Effect of AMG487 on DV2 replication in THP-1 cells. THP-1 cells were treated with DV2 without or with AMG487 (1 and 2.5 μM). **A.** The dsRNA expression (green) was measured using microscopy, bars in images $\sim 5 \mu\text{m}$. **B.** MFI of dsRNA was measured from Suppl. Fig. 5A and analyzed, ns= non-significant.

S7 Fig. AMG487 does not affect THP-1 cell survival. THP-1 cells were incubated with various concentrations of AMG487 for 16 hr. The tetrazolium dye MTT was added to culture to assess cell viability. The absorbance was measured at $\sim 500\text{nm}$ and percent cell viability was calculated from 2 independent experiments. Data presented as mean \pm SEM. One-Way ANOVA with multiple comparison test was used, *** $p < 0.05$. The 2.5 μM concentration did not affect the cell survival.

S8 Fig. Plasma PF4 inversely correlated with platelets counts in Dengue patients. The plasma PF4 (as mentioned in Fig. 4A) showed inverse relationship with platelet counts (as mentioned in Table S1) during Day3/5/9 in 8 patients, with a correlation coefficient, $r \sim -0.6642$.

S9 Fig. Gating strategy for detecting intracellular NS1 (viral) and CD41 (platelet) in monocytes from patients with dengue infection. As mentioned in Fig. 3B-C, the monocytes were isolated from patients' blood and stained for intracellular NS1 and CD41. Flow cytometry plot for 2 patients and a healthy individual is mentioned.

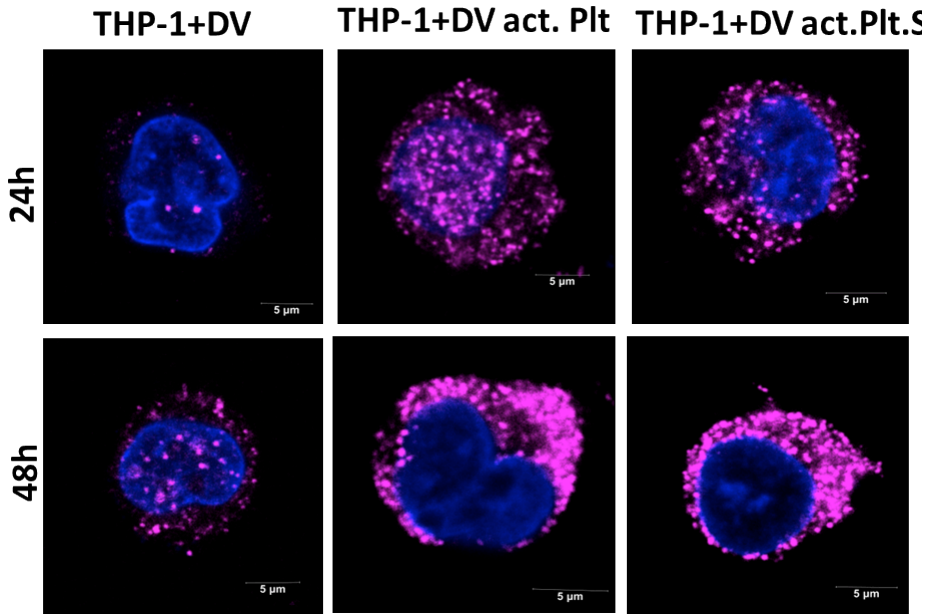
S10 Fig. The interferon-stimulated gene-15 or *ISG-15* expression was measured using qPCR from mice brain tissue from experiment-1. **A.** Represents data same mice from Fig. 6B1 and 6F1. **B.** Represents data from same mice from Fig. 6B2 and 6F2. Data present fold-change compared to mock. Data analyzed using One-Way ANOVA, *** $p < 0.0001$.

S1 Table. Brief information about DV patients. Data of plasma NS1 level and platelet counts are mentioned. P stands for positive, N ~ negative, Na ~ data not available. Platelet counts ~ $\times 10^3/\mu\text{L}$ plasma.

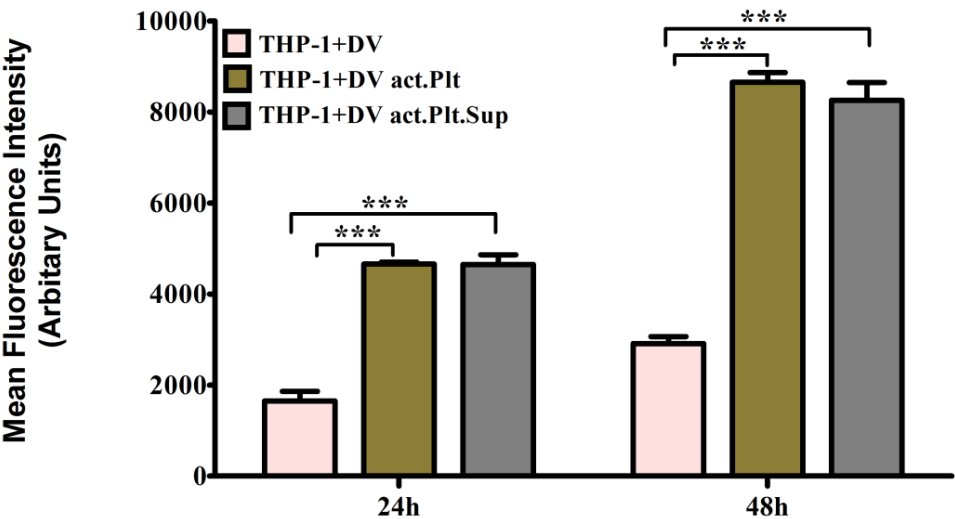
S2 Table. List of proteins identified from the proteomic data from post-nuclear fraction of THP-1 cells treated with: **A.** only DV2, **B.** DV2-activated platelets or **C.** untreated platelets. MASCOT score was calculated from 2 biological replicates and 3 technical replicates.

S3 Table. A. List of proteins found to be involved in viral infection (VI), viral replication (VR) and platelet proteins (PP), analyzed using Ingenuity pathway analysis (IPA) with threshold p value $< 3 \times 10^{-15}$. Platelet proteins enlisted were also analyzed through the PlateletWeb software. **B.** List of 7 common proteins in the above 3 groups, along with relative quantification NSAF score, analyzed through PeptideShaker software. Total two times the experiment was done and in 3 technical replicates, average NSAF score was calculated from both the experiments.

S1A Fig

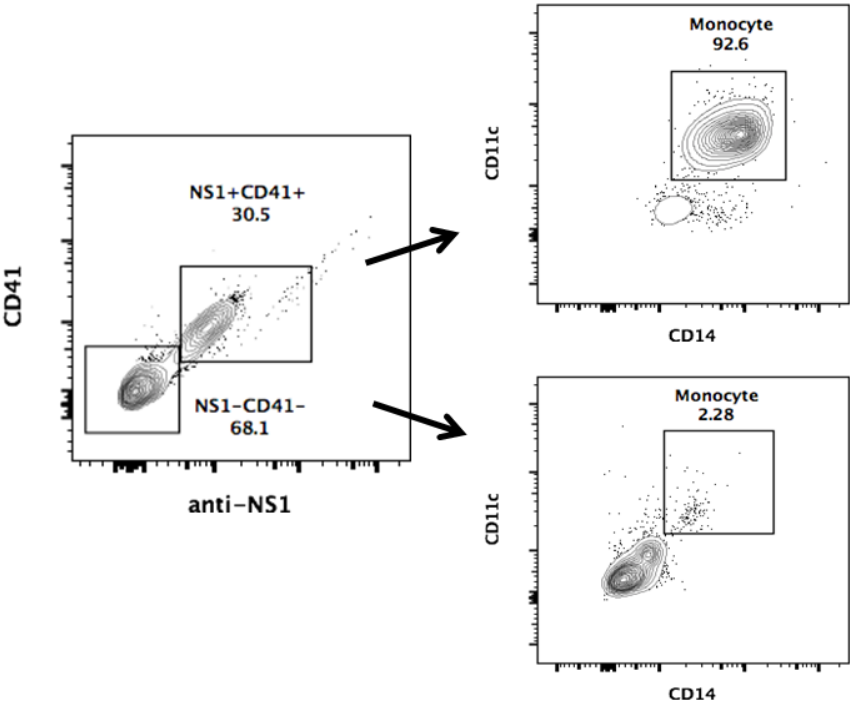


S1B Fig

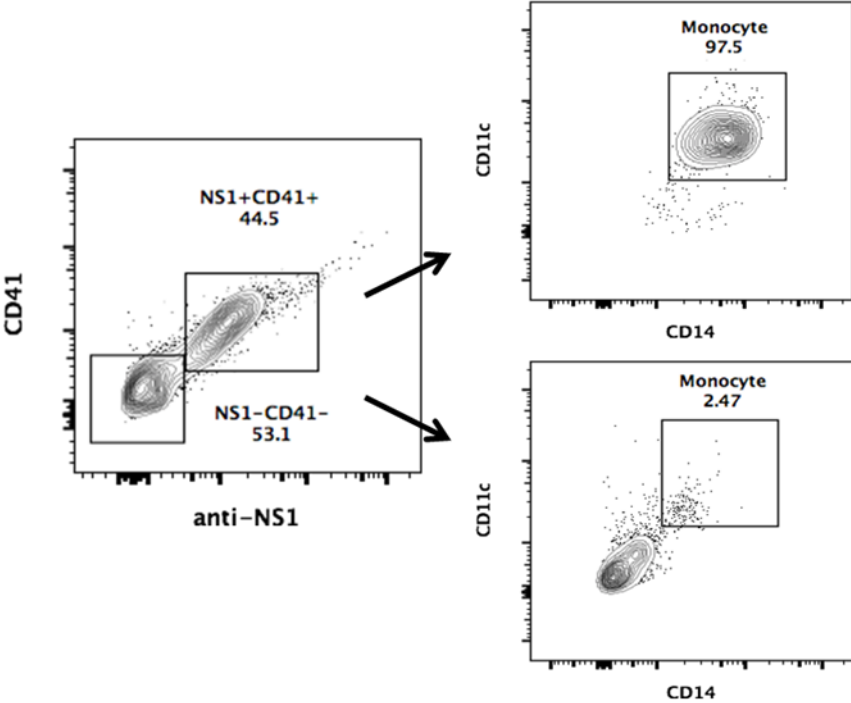


S2 Fig

Monocyte+NS1+Platelet (Low dose)

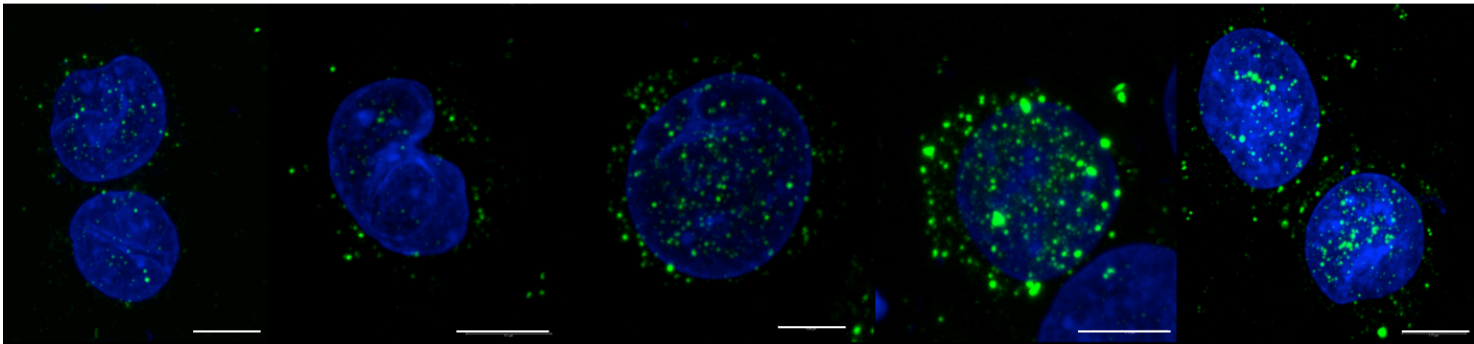


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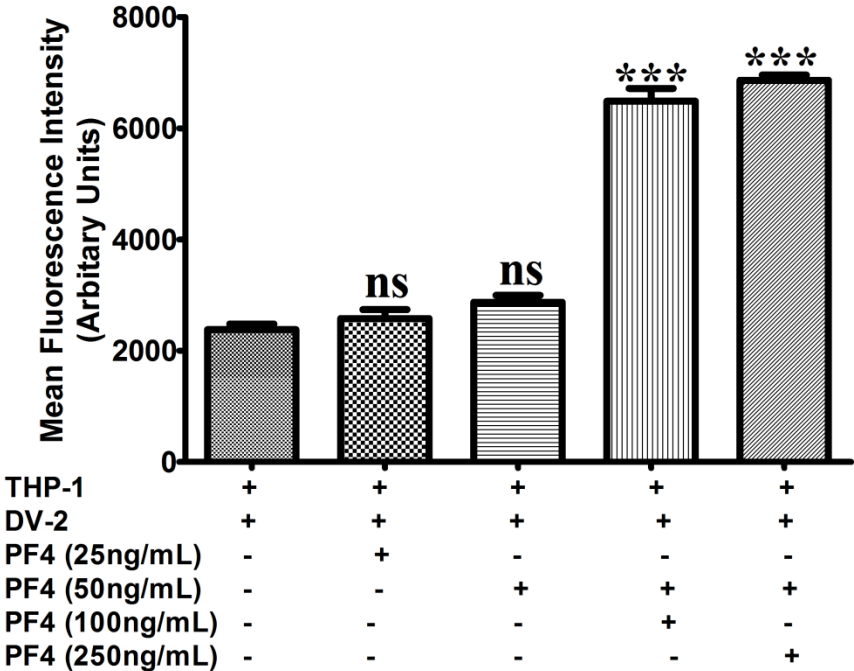


S3A Fig

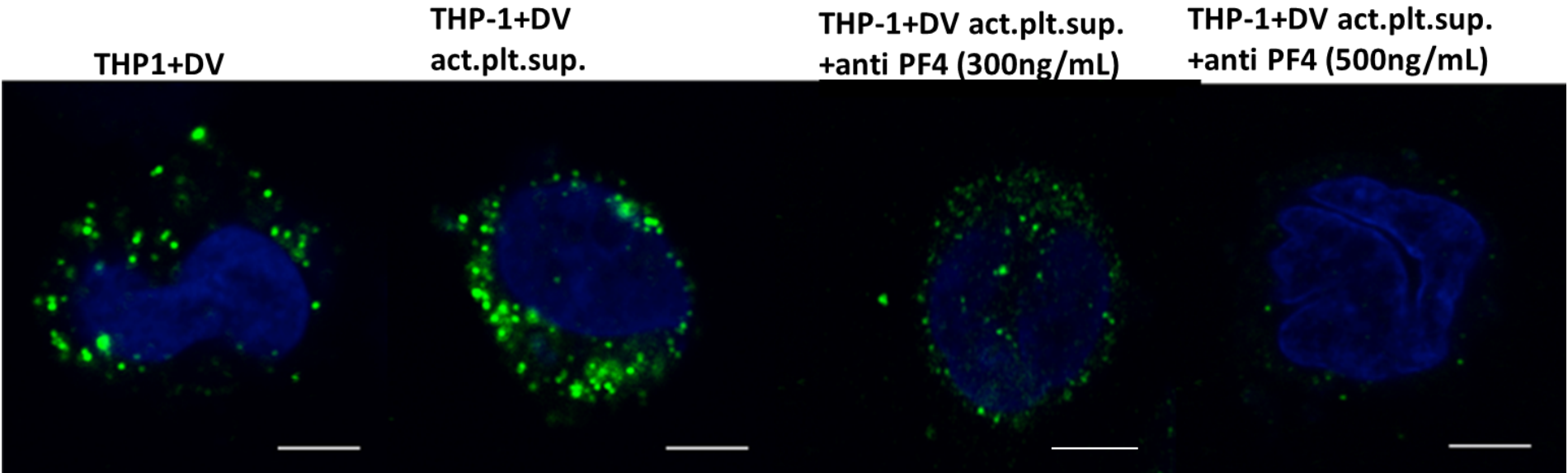
THP-1+DV THP-1+DV+PF4
 (25 ng/ml) THP-1+DV+PF4
 (50 ng/ml) THP-1+DV+PF4
 (100 ng/ml) THP-1+DV+PF4
 (250 ng/ml)



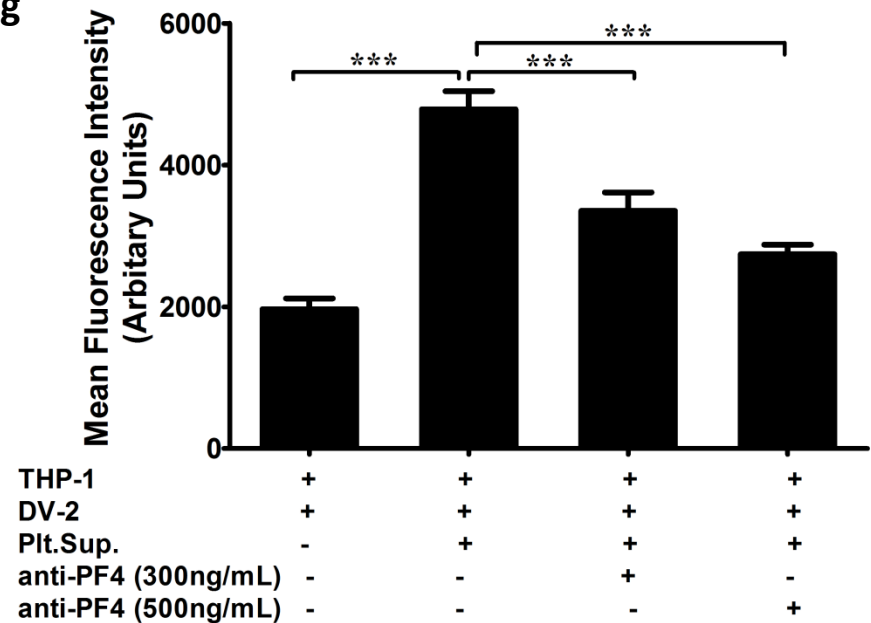
S3B Fig



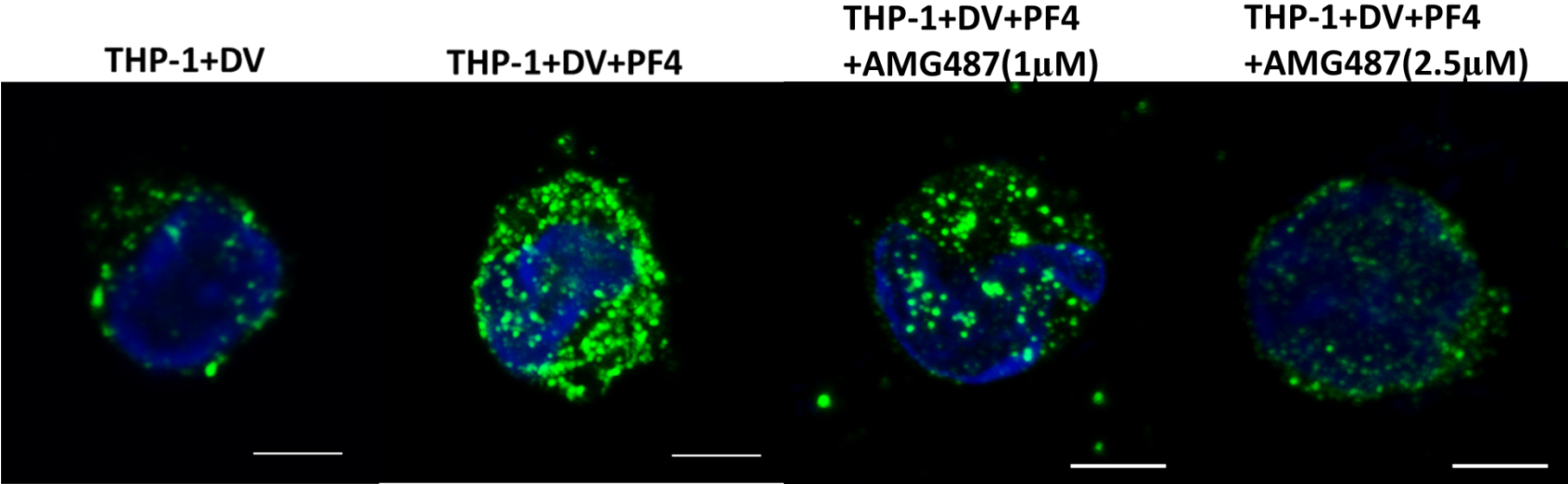
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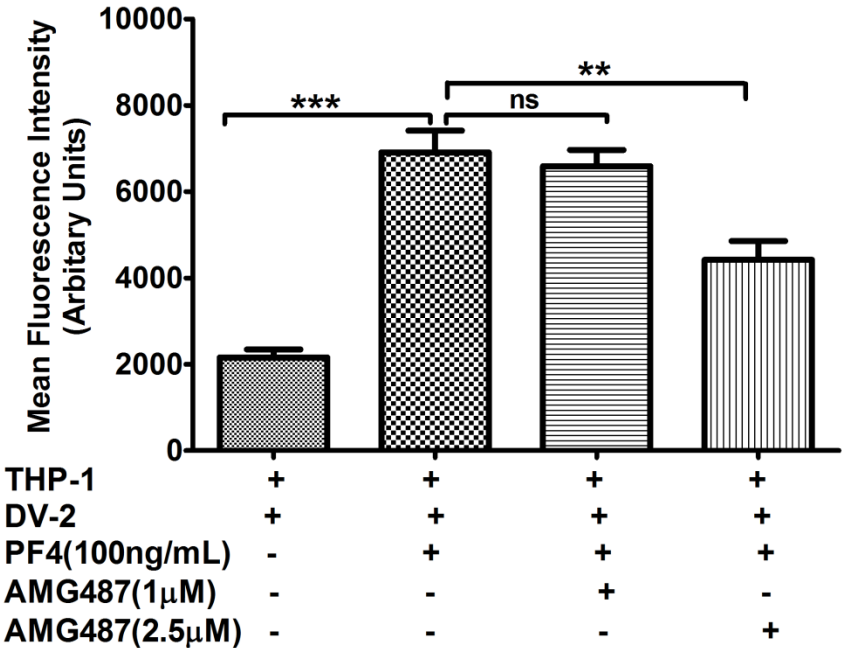
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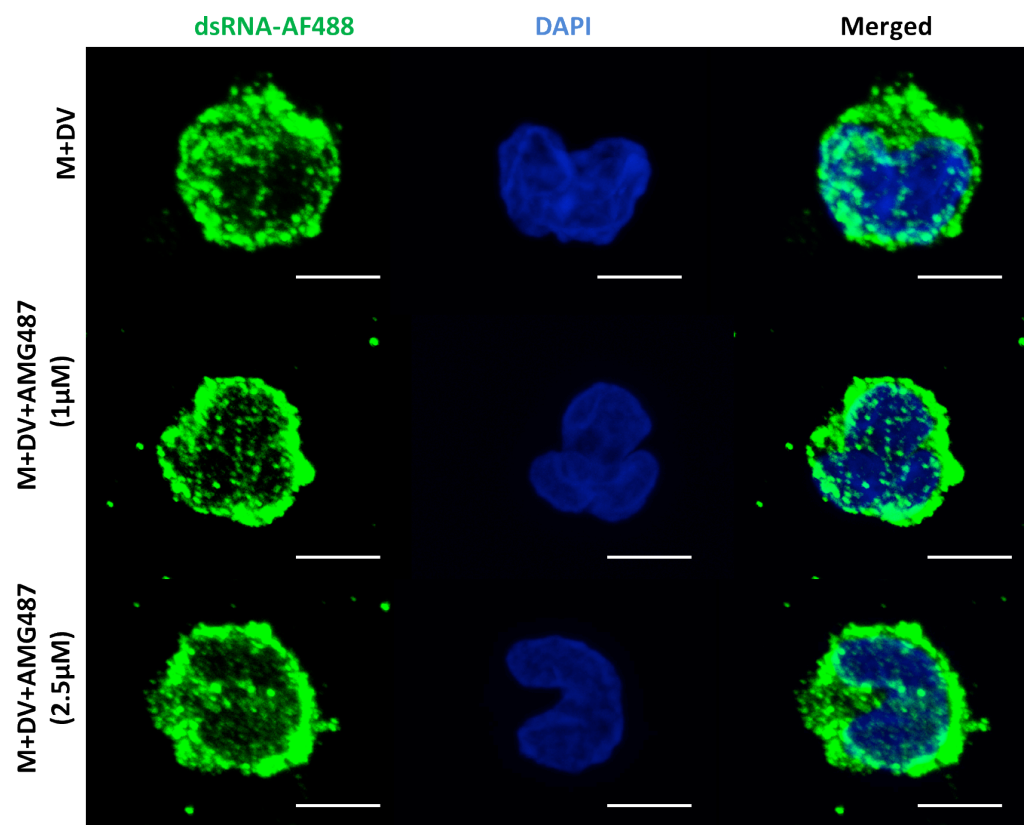
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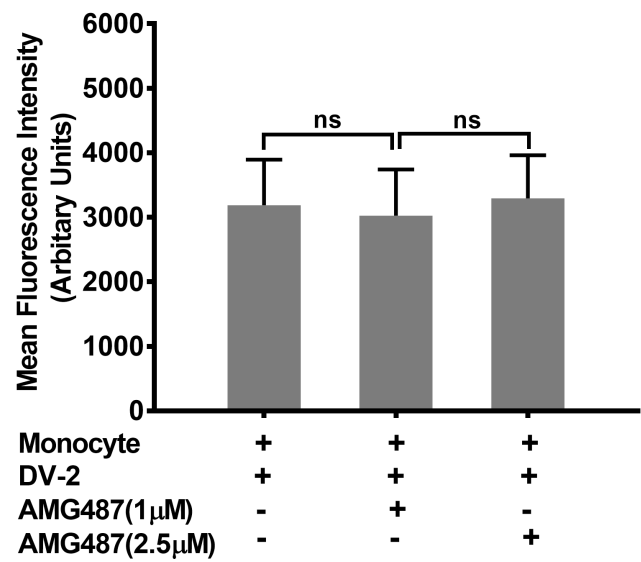
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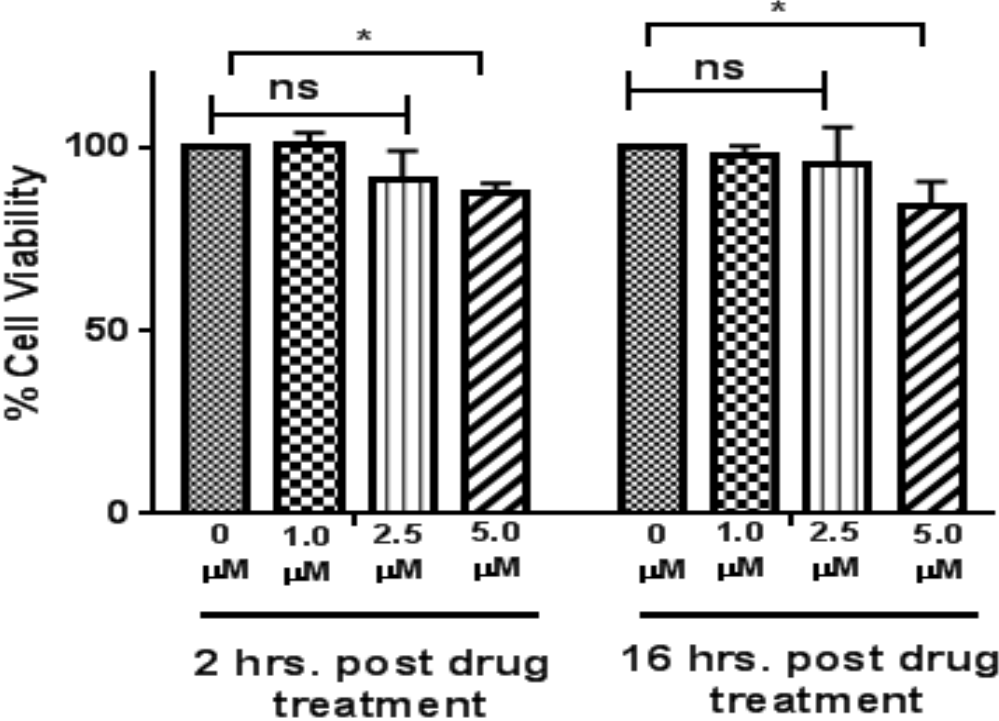
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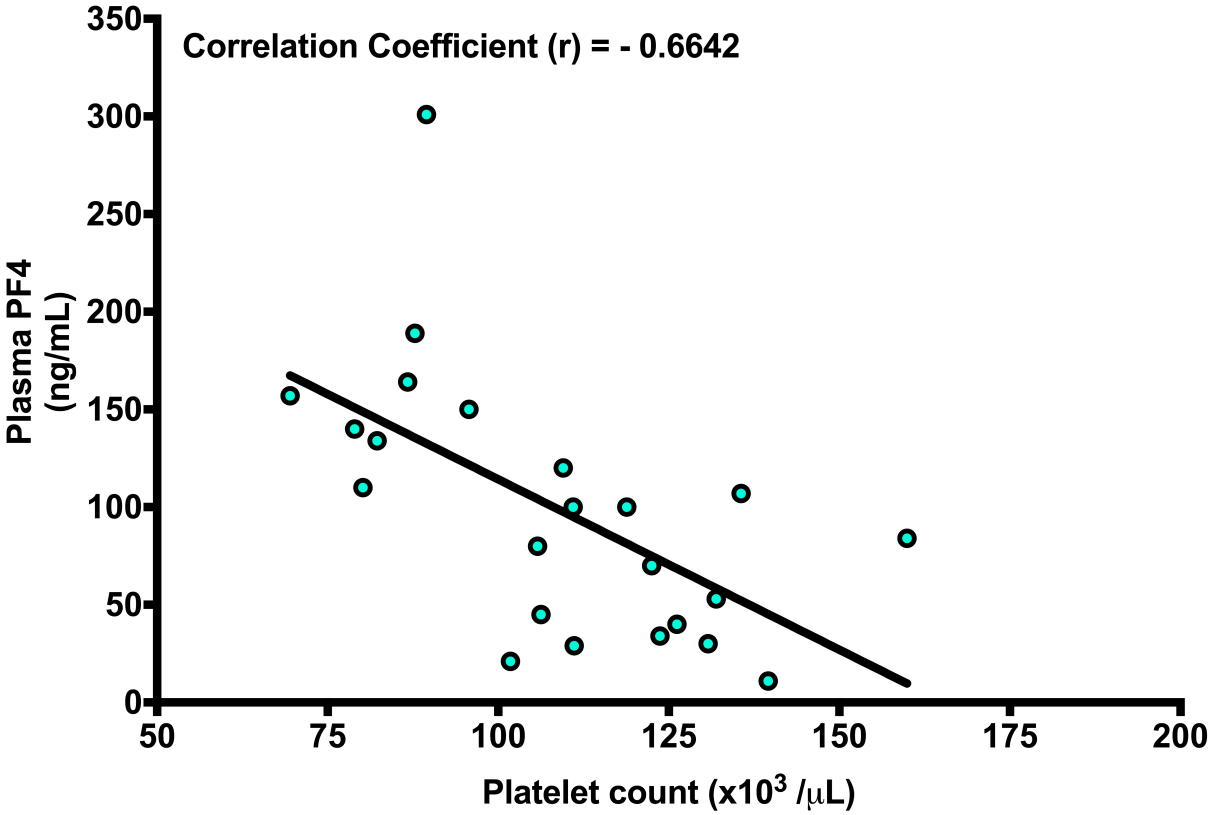
S6B Fig

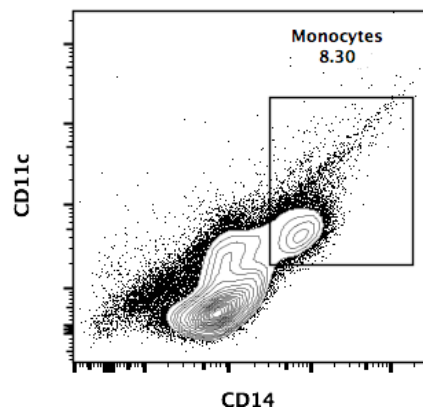
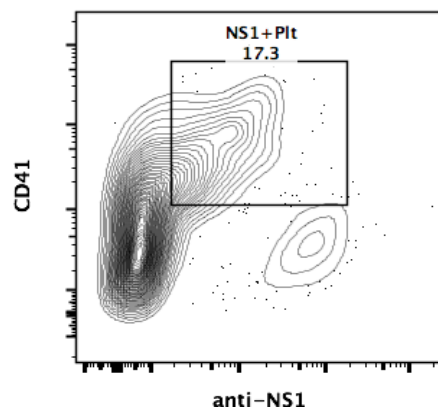
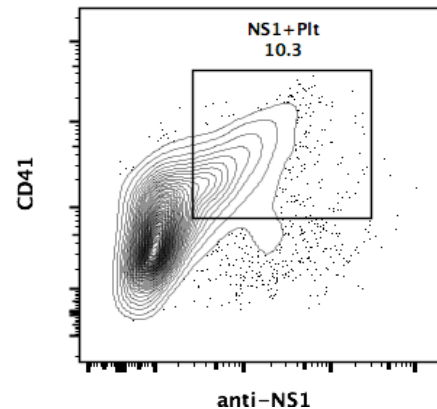
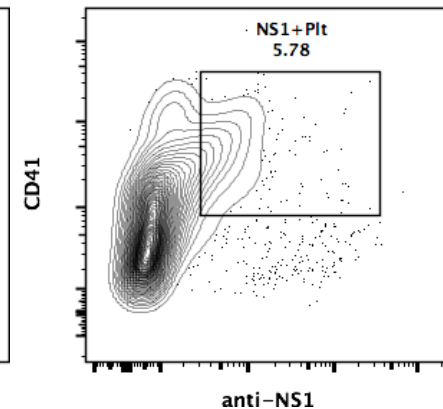
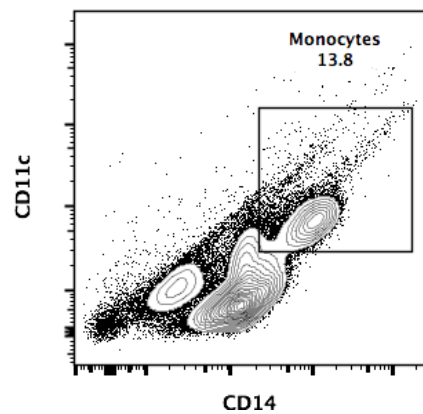
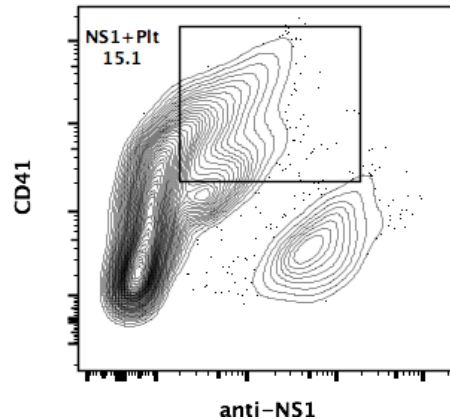
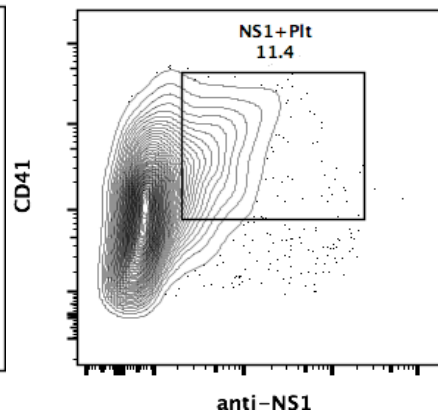
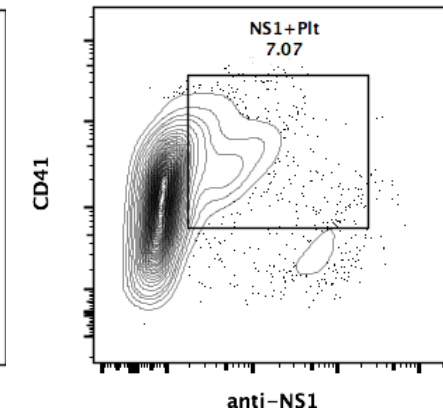
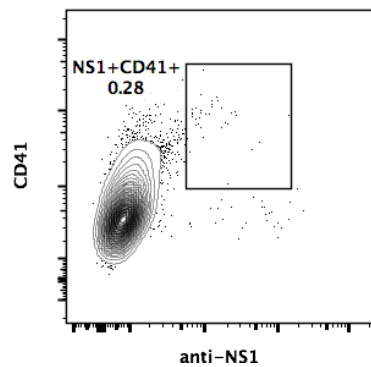
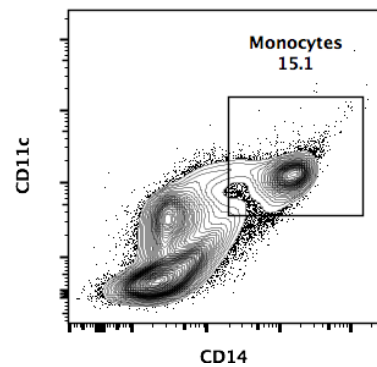


S7 Fig

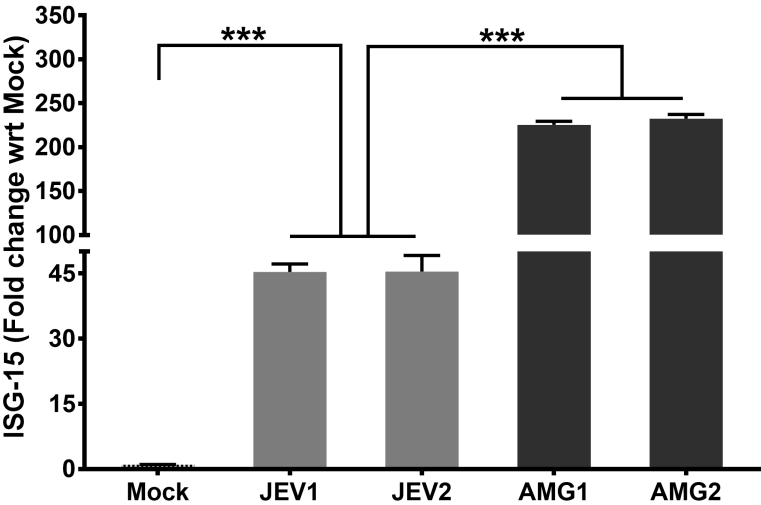


S8 Fig



S9 Fig**Patient-1****Day-3****Day-5****Day-9****Patient-2****Day-3****Day-5****Day-9****Control individual**

S10A Fig



S10B Fig

